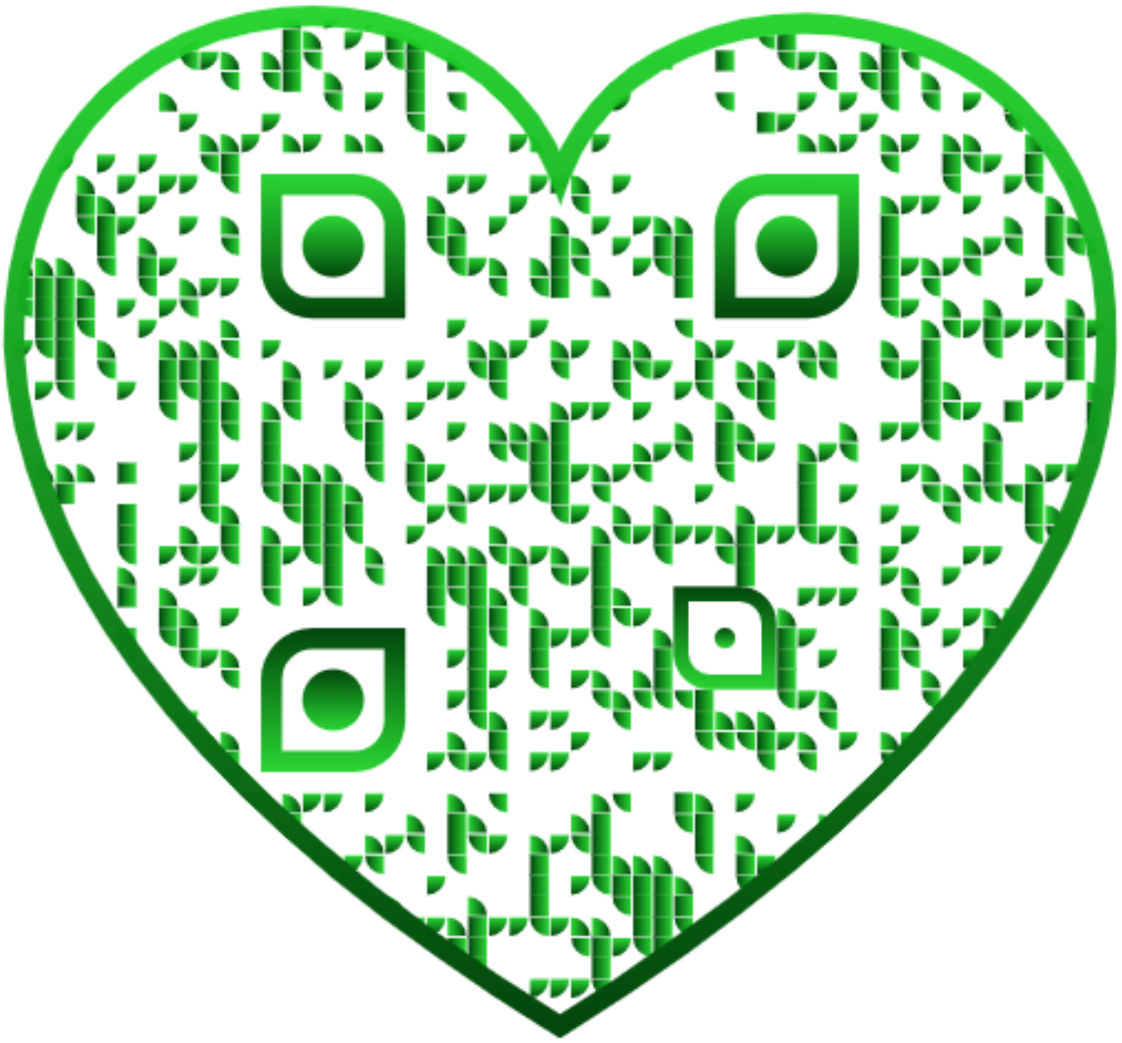
Draw Pharmacology in your mind

If you are a pharmacy student
If you are postgraduate and want to revise pharmacology by an easy way
If you are using any pharmacology reference
this file will aid you
> And wait for more <

Follow me at
Pharmacistalaanasr.wordpress.com
Contact me at
Pharm.alaa@gmail.com

لا تنسونى من صالح دعائكم

Pharmacist. **Alaa Nasr** د. آلاء نصر



Anxiolytics & Hypnotics

Alaa Nasr

- *Anxiety is a state of tension or fear of unknown reason*
- **Symptoms:** *Restlessness, GIT disturbance, Tachycardia, Sleep disturbance .. etc*
- ***So we use anxiolytics "Minor tranquilizers" at:***

→ **low doses** *to induce* ***anxiolysis***

→ **High doses** *to induce* ***sedation and hypnosis***

- **Limbic system (emotion) :** is responsible for **anxiety**
- **Reticular formation:** responsible for **wakefulness and hypnosis** *(remember, it contains locus cerulus)*
- **So how does hypnosis occur !**

→ Locus cerulus deliver sensation/stimulus (ex.hearing) to thalumus and cerebral cortex to integrate this sensation → hypnotics can block this action

Benzodiazepines

- The most widely used anxiolytics (49%)
- Safer than barbiturates

Mechanism

- They bind to $GABA_A$ receptors at the **BDZs binding site** → so ⇑ affinity of GABA to its receptor sites **causing:**
1. **More frequent opening of Cl^- channels**
2. **Hyperpolarization** and inhibition of neuronal activity

Actions

1. **⇓ Anxiety** → ⇓ activity in the limbic system → at low doses
2. **Sedation & hypnosis** → ⇓ activity in the reticular formation at high doses
3. **Anticonvulsant** action
4. **Muscle relaxation**

Pharmacokinetics

1. Well absorbed orally
2. Strongly bound to plasma proteins
3. Accumulated in body fats (⇑ lipid solubility)
4. Hepatic metabolism of some BDZs leads to an active metabolite → ⇑ $t_{1/2}$
5. **They don't cause acceleration of Cytochrome P_{450}**

Classification

Short-acting	3-8 hours	**Midazolam (Dormicum®)**-Oxazepam-Triazolam
Intermediate-acting	10-20 hours	**Alprazolam (Xanax®)**-Temazepam-Lorazepam
Long-acting	Up to 30 hours	**Diazepam (Valium®)**-Clonazepam-Flurazepam Chlorazepate - chlordiazepoxide

Uses

1. **Treatment of anxiety**
   - ♦ *If continued severe anxiety* → long-acting (Diazepam)
   - ♦ *If acute / panic disorder* → intermediate-acting (Alprazolam)
2. **Treatment of sleep disorders / insomnia**
   - ♦ *To ⇑ sleep duration* → long-acting
   - ♦ *To treat frequent awaking* → intermediate-acting
   - ♦ *To facilitate the start of sleeping* → short-acting
3. **Treatment of seizures**
   - ♦ **Clonazepam** → used for petit-mal epilepsy
   - ♦ **Diazepam** → *drug of choice* for grand-mal epilepsy / status epilepticus

∂ ***Note that ..*** BDZs can't be used to treat strychnine-induced convulsions

4. **Treatment of muscle disorders**
   - ♦ **Diazepam** → treatment of skeletal muscle spasms accompanying anxiety
5. **IV to induce anesthesia or as a pre-anesthetic medication** → as it causes *anterograde amnesia*

Adverse effects

1. **Drowsiness, confusion, cognition impairment**
2. **Ataxia** → impairment of motor coordination *(**takecare..** this affects manual skills like driving)*
3. **Anterograde amnesia**
4. **Shallow phase sleeping**
5. **Tolerance** → because of receptor downregulation
6. **Dependence** → (if suddenly stopped → anxiety, agitation, insomnia, tension)
7. **Acute over-dosage (suicidal attempts)**
   - ♦ **Symptoms:** prolonged sleeping
   - ♦ No serious signs of toxicity (like barbiturates)
   - ♦ There is a **specific antidote** for BDZs **Flumazenil**

Barbiturates

Mechanism

- **They ⇓ the activity in the reticular formation:**
1. ⇑ binding of GABA to GABA receptors
2. ⇑ effect of GABA on Cl^- conductance **by ⇑ the period of Cl^- channel opening**
3. GABA-mimetic action at high doses
4. ⇓ glutamate induced depolarization / stimulation

Actions

1. **CNS depression**
   - ♦ **Low doses** → sedation
   - ♦ **High doses** → hypnosis → anesthesia → respiratory depression → coma → **death**
2. **Cardiovascular inhibition** → ⇓ blood pressure → ⇓ heart rate → ⇓ cardiac output
3. **Induction of liver microsomal enzyme CYP_{450}** → leading to **tolerance**, **and ⇑ rate of metabolism** of barbiturates and other administered durgs

Pharmacokinetics

1. Well absorbed orally - Metabolized in liver - Excreted in urine
2. Some of them **(ex. Thiopental)** are highly lipid soluble → undergoes redistribution from the brain to adipose tissues → recovery occurs within minutes

Classification

Ultra short-acting	10-20 minutes	**Thiopental**
Short-acting	3-8 hours	**Pentobarbital - Secobarbital**
Long-acting	1-2 days	**Phenobarbital**

Uses

1. **Induction of anesthesia**
   - ♦ Ultra short-acting **(Thiopental)**
2. **Sedation and hypnosis**
   - ♦ Short-acting type but now is replaced by BDZs
3. **Treatment of seizures**
   - ♦ **Phenobarbital (long-acting)** → used for grand-mal epilepsy

∂ ***Note that ..*** Can be used to treat strychnine-induced convulsions

Adverse effects

1. **Drowsiness**
2. **Drug hang-over**
3. **Tolerance** → because of induction of LMEs
4. **Dependence** → (if suddenly stopped → ***Severe withdrawal symptoms*** → anxiety, tremors, restlessness, nausea, vomiting, seizures, cardiac arrest, **death**)
5. **Acute over-dosage (suicidal attempts)**
   - ♦ **Symptoms:** respiratory and C.V depression → **death**
   - ♦ **Treated by:** Artificial respiration, gastric lavage, forced alkaline diuresis (using $NaHCO_3$)
   - ♦ There is **no antidote**

Anxiolytics & Hypnotics

Alaa Nasr

Beta blockers

♦ **Example: Propranolol (Indral®)**

♦ They ⇓ peripheral sympathetic responses associated with anxiety → ⇓ physical symptoms → tachycardia, sweating, tremors → so **only considered as anxiolytics but not hypnotics**

♦ **Used in case of stage fright**

5HT1A agonists

♦ **Example: Buspirone (Buspar®)**

They interfere with arousal reactions

♦ **Differences from BDZs:**

1. Don't affect GABA receptors

2. Don't cause sedation, ataxia, or withdrawal symptoms

Side effects: Nausea, dizziness, headache

Others

Hydroxyzine

♦ **(Atarax®)**

♦ 1st generation antihistaminic with antiemetic properties

♦ **Used mainly now as sedative**

♦ Has tendency for habituation

♦ **Suitable for** patients with anxiety *having a history of drug abuse*

Zolpidem & Zaleplon

♦ **(Stilnox®) (Sleep aid®)**

♦ Potent non-BDZs hypnotics

Advantages

1. No muscle relaxing properties
2. Minimal rebound insomnia
3. No tolerance and withdrawal symptoms

Disadvantages

1. GIT disturbances
2. **Nightmares**
3. Headache and dizziness

Kava Kava

♦ **(Kava®)**

♦ Its action is through affecting $GABA_A$ receptors in the brain

♦ **It is hepatotoxic so should be discontinued in less than 2 months even if it is effective**